GEI-078

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	:	M. Hul
M. LANQUETIN et al	:	
Serial No.: 09/646,763	:	Group: 1617
Filed: September 20, 2000	:	
For: TOPICAL HORMONAL...ACTION	:	

475 Park Avenue South
New York, N.Y. 10016
November 25, 2003

BRIEF ON APPEAL

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REAL PARTY IN INTEREST

The real party in interest is Laboratoire Theramex S.A. by means of an assignment recorded in the United States Patent Office.

RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to Appellant, the Appellant's legal representative, or assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

STATUS OF THE CLAIMS

The claims in the application are claims 1, 3 and 5 to 18, all other claims having been cancelled.

STATUS OF AMENDMENTS

There were no amendments filed subsequent to the final rejection of December 17, 2002.

SUMMARY OF THE INVENTION

The present invention is drawn to a topical hormonal composition having a systemic effect for the correction of progesterone deficiency in premonopausal women and for hormone replacement in menopausal women containing as the active ingredient nomegesterol and esters and ethers thereof, a vehicle permitting systemic passage of the active ingredient selected from the group consisting of a solubilizing agent and an absorption promoter, a film forming agent and a gelling agent or mixtures thereof combined with a suitable excipient to produce a gelled or film-forming pharmaceutical which compositions are for systemic use and not topical use.

THE PRIOR ART

Saunal et al	6,010,716	January 2000
Eibl et al	5,290,769	May 1994
Winters et al	WO-95/304409	November 1995

Gennaro et al Remingtons Pharmaceutical Sciences (1990), page 1305

Merk Index, 12th Edition, 1996; pages 889-890, Compound 5232

Maillo et al	EP 0,785,211	July 1997

THE ISSUES

Claims 1, 3, 5 to 8, 11, 12, 14, 15 and 18 have been rejected under 35 USC 103 as being obvious over the Saunal et al reference and Maillo et al '211 taken in view of the Winters '409 reference. Claims 9, 10, 13, 16 and 17 have been rejected under 35 USC 103 as being obvious over the same prior art taken in further view of the Merck Index, the Eibl et al patent and Remington's Pharmaceutical Sciences reference. The Examiner states that the Saunal et al reference teaches a transdermal topical formulation using a solvent and absorption promoting agent, an active steroid and a film-forming agent while Winters et al allegedly teaches a topical formulation of 19-nor progesterone for systemic delivery of the active ingredient having a solvent film-forming agent and cellulose in a plasticizing agent. The Examiner concedes that the primary references do not teach the

use of preferred carrier materials of propyleneglycol and the like and that they do not teach the weight ratio of nomegesterol to be 0.05 to 1% by weight and do not teach the specific ratios.

The Examiner cites the Eibl et al patent as teaching propyleneglycol and copolymers of methacrylic acid and ethyl acrylate as being an auxiliary agent for pharmaceuticals and topical formulations. The Merck Index is cited to show that isopropylpropylidene glycerol my be used as a plasticizing agent and the Remington Sciences reference is cited to show that carbomer is useful as a gelling and emulsifying agent and therefore, deems that the claimed compositions would be obvious.

GROUPING OF THE CLAIMS

The claims stand or fall together.

APPLICANTS' ARGUMENTS

Applicants respectfully request the Board of Patent Appeals and Interferences to reverse the Examiner's rejection since the combination of the prior art that the Examiner has made with the benefit of Applicants' disclosure would not suggest Applicants' invention to one skilled in the art, particularly since there is no suggestion or teaching to

combine the references as the Examiner has done with the benefit of Applicants' disclosure. The Saunal et al patent relates to compositions for transdermal delivery of an active ingredient which could possibly be nomegesterol acetate and optionally a polymeric release matrix capable of forming a flexible film when dried which matrix is selected from the group consisting of cellulose polymers or copolymers, vinyl-pyrrolidene, vinyl acetate copolymers and a physiologically non-aqueous solvent to dissolve the release matrix and the transcutaneous absorption promoter by quickly removing the same by evaporation from the skin.

Transdermal compositions are completely different from a gel with systemic activity. Transdermal compositions are made of a small reservoir fixed to a strip of plastic material and the reservoir is then placed against the skin. The reservoir normally contains a large amount of an active ingredient dissolved in a lipophilic diluent and the active ingredient diffuses through the skin from the lipophilic phase. The objective of such a preparation is to have a delayed or protracted diffusion of the active ingredient through the skin and a transdermal device is not intended to have the product reach the bloodstream as in Applicants' composition but is intended to diffuse the active ingredient from the reservoir through the skin. The compounds present in the reservoir are selected due to their high lipophilicity and includes compounds such as estradiol, scopolamine, nicotine and the like.

Applicants formulation, as noted above, has absolutely nothing to do with a transdermal application since Applicants' invention is intended to ensure passage of the active ingredient nomegesterol acetate into the bloodstream and therefore, the Saunal et al patent in no way relates to Applicants' invention.

The Maillos et al reference relates to 19-nor pregnane derivatives which are potent progestogens devoid of residual androgenic activity. The reference teaches oral administration but also parental administration, intramuscular subcutaneous and percutaneous and vaginal, ocular or nasal roots in the form of solid, semi-solid or liquid dosage form and refers to all pharmaceutical compositions generally but does not teach Applicants' compositions.

The Winters et al reference does not overcome the deficiencies of the primary references as it is directed to a topical polymeric drug delivery system to deliver drugs to the skin topically by the use of a propellant free airless pump for the deliver which has absolutely nothing to do with Applicants' invention. The tertiary references do not overcome the deficiencies of the primary and secondary references and one skilled in the art would not combine the same to obtain Applicants' novel compositions with their novel activity.

Synthetic progesterones have the main drawback of having very poor diffusion properties through the skin due to their lipophilic character and Applicants' invention provides a precise balance between the solubility of the active ingredient and the vehicle and its ability to diffuse through the skin towards the bloodstream. This is why the mixture proportion of the preferred solubilizing agent suitable for Applicants' invetnion is the main point of distinction with respect to the prior art. The effectiveness of the composition is the result of the proper combination and term of dosage of all the excipients.

In Applicants' invention, the preferred solubilizing agent is a ternary mixture or a quaternary mixture of 95% ethanol/water/propyleneglycol and optionally Labrasol wherein the percentage of 95% ethanol varies from 30 to 50% and the amount of water is 30 to 60% and the propyleneglycol is 2 to 20% and the Labrasol is 3 to 7%, all percentages being by weight. This composition permits nomegesterol to pass through the cutaneous barrier to obtain good clinical results when the excipient mixture proportions are properly balanced as can be seen from the examples in the application as filed.

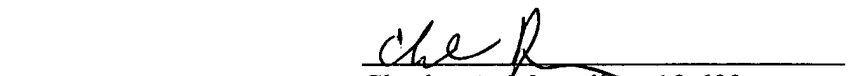
The Saunal et al compositions do not contain propylene glycol which contributes to the effectiveness of the diffusion through the skin and Saunal et al did not show any examples of compositions containing 19-nor progesterone derivatives and specifically not nomegesterol acetate. The reference taught estradiol compositions as being easily

obtained and satisfactorily efficient due to the high lipophilicity of estradiol. Saunal et al only postulates the possibility that these compositions could contain nomegesterol acetate and does not teach Applicants' advantages of the compositions. There is no way to obtain Applicants' gel having systemic activity with the active ingredients being highly lipophlic.

CONCLUSION

Applicants respectfully request the Board of Patent Appeals and Interferences to reverse the Examiner's rejection since it is deemed that the claims clearly point out Applicants' patentable contribution over the prior art cited by the Examiner. Therefore, Applicants have complied with all the necessary requisites for the granting of a Letters Patent. Three copies of the brief on appeal are being together with PTO Form-2038 authorizing the $330.00 fee for filing the appeal brief.

Respectfully submitted,
Muserlian, Lucas and Mercanti



Charles A. Muserlian, 19,683
Attorney for Applicants
Tel. # (212) 661-8000

CAM:ds
Enclosures

GEI-078

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	:	M. Hul
M. LANQUETIN et al	:	
Serial No.: 09/646,763	:	Group: 1617
Filed: September 20, 2000	:	
For: TOPICAL HORMONAL...ACTION	:	

475 Park Avenue South
New York, N.Y. 10016
November 25, 2003

APPENDIX

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The claims on appeal are as follows:

Claim 1 (previously presented)

A gelled and/or film-forming topical hormonal composition with systemic effect for treating progesterone deficiency in pre-menopausal women and for hormone replacement in menopausal women comprising a) 0.05 to 1% by weight of the composition of at least one active principle selected from the group consisting of nomegestrol, and ethers and esters thereof, b) at least one vehicle permitting systemic passage of a solubilizing agent, an absorption promoter, a film-forming agent and a gelling agent and c) optionally a diluent.

Claim 2 (cancelled)

Claim 3 (previously presented)

A topical hormonal composition with systemic effect of claim 1 wherein nomegestrol acetate is used.

Claim 4 (cancelled)

Claim 5 (previously presented)

A topical hormonal composition with systemic effect of claim 1 wherein the quantity of nomegestrol or of one of its esters or ethers is about 0.4% by weight of the total composition.

Claim 6 (previously presented)

A topical hormonal composition with system effect of claim 1 containing at least one solubilizng agent selected from the group consisting of water, alcohols, propyleneglycol and C_8/C_{10} of polyoxyethylene glycosyl glyceride.

Claim 7 (previously presented)

A topical hormonal composition with systemic effect of claim 1 wherein the solubilizing agent is a ternary mixture of 95% ethanol/water/propyleneglycol, in which the percentage of 95% ethanol is 30 to 50%, that of water is 30 to 60% and that of propyleneglycol is 2 to 20%.

Claim 8 (previously presented)

A topical hormonal composition with systemic effect of claim 1 containing a solubilizing agent of quaternary mixture of 95% ethanol/water/C_8/C_{10} of polyoxyethylene glycosyl glyceride, propyleneglycol, in w hich the percentage of 95% ethanol is 30 to 50%, that of water is 30 to 60%, that of the glyceride is 3 to 7% and that of propyleneglycol is 2 to 20%.

Claim 9 (previously presented)

A topical hormonal composition with system effect of claim 1 containing an absorption promoter selected from the group consisting of isopropylideneglycerol, α-tocopheryl polyethyleneglyco. 1000 succinate and monoethyl ether of diethylene glycerol.

Claim 10 (previously presented)

A topical hormonal composition with systemic effect of claim 9 wherein the absorption promoter is isopropylideneglycerol.

Claim 11 (previously presented)

A topical composition with systemic effect of claim 1 containing a gelling agent selected from the group consisting of cellulose derivatives selected from the group consisting of

methylcelluloses,

ethylcelluloses (Ethocel),

hydroxypropylmethylcelluloses,

hydroxyethylcelluloses,

hydroxypropylcelluloses and

carboxymethylcelluloses in the sodium or calcium form

and acrylic carbomer.

Claim 12 (previously presented)

A topical hormonal composition with system effect of claim 11 containing hydroxypropylmethyl-cellulose.

Claim 13 (previously presented)

A topical hormonal composition with systemic effect of claim 11 containing a carbomer.

Claim 14 (previously presented)

A topical hormonal composition with systemic effect of claim 1 containing a film-forming agent selected from the group consisting of cellulose, acrylic, methacrylic acid copolymers and polyvinylpyrrolidone.

Claim 15 (previously presented)

A topical hormonal composition with systemic effect of claim 14 containing hydroxypropylmetnylcellulose acetate succinate.

Claim 16 (previously presented)

A topical hormonal composition with systemic effect of claim 14 containing an aqueous dispersion of an anionic copolymer of methacrylic acid and ethyl acrylate as the film-forming agent.

Claim 17 (previously presented)

A topical hormonal composition with systemic effect of claim 1 in the form of a gel or a film-forming gel containing an aqueous-alcoholic mixture with 8% of propyleneglycol and 3% of isopropylidene glycerol.

Claim 18 (previously presented)

A method of systemically effecting correction of progesterone deficiency in premenopausal women comprising administering to premenopausal women in need thereof a systemically correcting amount of a composition of claim 1 to treat progesterone deficiency.